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SDIs in CAPlus
NEWS 6 May 27 CAPlus super roles and document types searchable in REGISTRY
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NEWS EXPRESS MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
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FILE 'HOME' ENTERED AT 16:21:59 ON 14 JUL 2004

=> file medline biosis embase caplus
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.21	0.21

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 16:22:08 ON 14 JUL 2004

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=> s schwartz david a/au
L1 309 SCHWARTZ DAVID A/AU

=> s schutte brian c /au
L2 117 SCHUTTE BRIAN C

=> lorenz eva/au
LORENZ IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s lorenz eva/au
L3 51 LORENZ EVA/AU

=> s tlr4 (s) polymorph
=>
=> s tlr4 (s) polymorphism
L4 197 TLR4 (S) POLYMORPHISM

=> s tlr4 (s) polymorphism (s) amino
L5 5 TLR4 (S) POLYMORPHISM (S) AMINO

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6 2 DUP REM L5 (3 DUPLICATES REMOVED)

=> d l6 total ibib kwic

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:696329 CAPLUS
DOCUMENT NUMBER: 136:229883
TITLE: Excess of rare amino acid polymorphisms in the
Toll-like receptor 4 in humans
AUTHOR(S): Smirnova, Irina; Hamblin, Martha T.; McBride, Colleen;
Beutler, Bruce; Di Rienzo, Anna
CORPORATE SOURCE: Department of Internal Medicine and the Howard Hughes
Medical Institute, University of Texas Southwestern
Medical Center, Dallas, TX, 75390, USA
SOURCE: Genetics (2001), 158(4), 1657-1664
CODEN: GENTAE; ISSN: 0016-6731
PUBLISHER: Genetics Society of America
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT Gene, animal
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(TLR4; rare amino acid polymorphisms
excess in Toll-like receptor 4 in humans)

L6 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001446631 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11494169
TITLE: A functional polymorphism of toll-like receptor 4 is not
associated with likelihood or severity of meningococcal
disease.
COMMENT: Comment in: J Infect Dis. 2003 Jan 15;187(2):341-2; author
reply 342-3. PubMed ID: 12552467

AUTHOR: Read R C; Pullin J; Gregory S; Borrow R; Kaczmariski E B; di
 Giovine F S; Dower S K; Cannings C; Wilson A G
 CORPORATE SOURCE: Division of Genomic Medicine, Royal Hallamshire Hospital,
 University of Sheffield, Sheffield S10 2RX, United
 Kingdom.. r.c.read@shef.ac.uk
 SOURCE: Journal of infectious diseases, (2001 Sep 1) 184 (5) 640-2.
 Journal code: 0413675. ISSN: 0022-1899.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 200109
 ENTRY DATE: Entered STN: 20010813
 Last Updated on STN: 20030221
 Entered Medline: 20010920

AB . . . (TLR4) transduces proinflammatory cytokine release by human cells
 in response to lipopolysaccharide (LPS). This study tested the hypothesis
 that, if **TLR4** is rate limiting for a successful response to
 bacterial LPS in humans, a human gene **polymorphism** that results
 in the **amino** acid substitution Asp299Gly and causes reduced
 expression and function of **TLR4** should influence susceptibility
 to or severity of natural gram-negative infection. The allele frequency
 of the Asp299Gly polymorphism was 5.9% among. . .

=> d his

(FILE 'HOME' ENTERED AT 16:21:59 ON 14 JUL 2004)

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 16:22:08 ON 14 JUL 2004

L1 309 S SCHWARTZ DAVID A/AU
 L2 117 S SCHUTTE BRIAN C /AU
 L3 51 S LORENZ EVA/AU
 L4 197 S TLR4 (S) POLYMORPHISM
 L5 5 S TLR4 (S) POLYMORPHISM (S) AMINO
 L6 2 DUP REM L5 (3 DUPLICATES REMOVED)

=> dup rem l4

PROCESSING COMPLETED FOR L4

L7 96 DUP REM L4 (101 DUPLICATES REMOVED)

=> s tlr4 (s) polymorphism (s) immun8

8 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.
 For a list of commands available to you in the current file, enter
 "HELP COMMANDS" at an arrow prompt (=>).

=> s tlr4 (s) polymorph? (s) immun?

3 FILES SEARCHED...

L8 33 TLR4 (S) POLYMORPH? (S) IMMUN?

=> dup rem l8

PROCESSING COMPLETED FOR L8

L9 28 DUP REM L8 (5 DUPLICATES REMOVED)

=> d l9 total ibib kwic

L9 ANSWER 1 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
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ACCESSION NUMBER: 2004174142 EMBASE

TITLE: Sequence Variants of Toll-Like Receptor 4 Are Associated
 with Prostate Cancer Risk: Results from the Cancer Prostate
 in Sweden Study.

AUTHOR: Zheng S.L.; Augustsson-Balter K.; Chang B.; Hedelin M.; Li
 L.; Adami H.-O.; Bensen J.; Li G.; Johnasson J.-E.; Turner

A.R.; Adams T.S.; Meyers D.A.; Isaacs W.B.; Xu J.; Gronberg H.
CORPORATE SOURCE: J. Xu, Wake Forest Univ. School of Medicine, Medical Center
Blvd, Winston-Salem, NC 27157, United States.
jxu@wfubmc.edu
SOURCE: Cancer Research, (15 Apr 2004) 64/8 (2918-2922).
Refs: 23
ISSN: 0008-5472 CODEN: CNREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB sequence variants in genes that regulate inflammation may modify individual susceptibility to prostate cancer. The lipopolysaccharide receptor Toll-like receptor 4 (TLR4) is a central player in the signaling pathways of the innate immune response to infection by Gram-negative bacteria and is an important candidate inflammatory gene. We performed a systematic genetic analysis of TLR4 sequence variants by evaluating eight single-nucleotide polymorphisms that span the entire gene among 1383 newly diagnosed prostate cancer patients and 780 age- and residence-matched controls in Sweden. We found an association between a sequence variant (11381G/C) in the 3'-untranslated region of the TLR4 gene and prostate cancer risk. The frequency of the variant genotypes (CG or CC) was significantly higher in the patients. . . . the age of 65 years was even higher (26.3%). Compared with men who had the wild-type genotype of this single-nucleotide polymorphism (GG), those with GC or CC genotypes had a 26% increased risk for prostate cancer (odds ratio, 1.26; 95% confidence. . . .

L9 ANSWER 2 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
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ACCESSION NUMBER: 2004235753 EMBASE
TITLE: Association between common toll-like receptor 4 mutations and severe respiratory syncytial virus disease.
AUTHOR: Tal G.; Mandelberg A.; Dalal I.; Cesar K.; Somekh E.; Tal A.; Oron A.; Itskovich S.; Ballin A.; Hourri S.; Beigelman A.; Lider O.; Rechavi G.; Amariglio N.
CORPORATE SOURCE: Dr. I. Dalal, Dept. of Pediatrics, E. Wolfson Medical Center, Holon 58100, Israel. ilandalal@hotmail.com
SOURCE: Journal of Infectious Diseases, (1 Apr 2004) 189/11 (2057-2063).
Refs: 39
ISSN: 0022-1899 CODEN: JIDIAQ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB is extremely variable. Thus, it is likely that factors such as genetic heterogeneity contribute to disease severity. Toll-like receptor 4 (TLR4) and CD14 are part of a receptor complex involved in the innate immune response to RSV. Methods. The association of the TLR4 mutations (Asp299Gly and Thr399Ile) and the CD14/-159 polymorphism were analyzed in 99 infants hospitalized with severe RSV bronchiolitis (group I). Eighty-two ambulatory infants with mild RSV bronchiolitis (group II) and 90 healthy adults (group III) composed the 2 control groups. The TLR4 mutations and the CD14/-159 polymorphism were genotyped by use of reverse-transcriptase polymerase chain reaction and restriction fragment-length

polymorphism analysis, respectively. Results. Each of the **TLR4** mutations, either alone or in cosegregation, were associated with severe RSV bronchiolitis: the Asp299Gly and Thr399Ile mutations were significantly overrepresented in group I, compared with groups II and III. No association between the CD14/-159 **polymorphism** and RSV bronchiolitis was found. Conclusions. These findings suggest that **TLR4** mutations, but not the CD14/-159 **polymorphism**, are associated with an increased risk of severe RSV bronchiolitis in previously healthy infants.

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ACCESSION NUMBER: 2004123512 EMBASE
TITLE: Toll-like receptor 2 as a major gene for asthma in children of European farmers.
AUTHOR: Eder W.; Klimecki W.; Yu L.; Von Mutius E.; Riedler J.; Braun-Fahrlander C.; Nowak D.; Martinez F.D.
CORPORATE SOURCE: Dr. F.D. Martinez, Arizona Respiratory Center, University of Arizona, 1501 N Campbell Ave, Tucson, AZ 85724, United States
SOURCE: Journal of Allergy and Clinical Immunology, (2004) 113/3 (482-488).
Refs: 31
ISSN: 0091-6749 CODEN: JACIBY
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB . . . Is less frequent in children raised on animal farms has led to the conjecture that exposure to microbial products modifies **immune** responses. The toll-like receptors (TLRs) represent an evolutionarily conserved family of innate **immunity** receptors with microbial molecules as ligands. Objectives: We reasoned that **polymorphisms** in genes encoding TLRs might modulate the protective effects observed in farming populations. Methods: Farmers' and nonfarmers' children living in . . . rural areas in Austria and Germany and who were enrolled in the cross-sectional ALEX study were genotyped for single nucleotide **polymorphisms** in the TLR2 and **TLR4** genes. The frequencies of asthma, allergic rhinitis, and atopic sensitization were compared between the genotypes in relation to exposure to. . .

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ACCESSION NUMBER: 2004115837 EMBASE
TITLE: Highly purified lipoteichoic acid activates neutrophil granulocytes and delays their spontaneous apoptosis via CD14 and TLR2.
AUTHOR: Lotz S.; Aga E.; Wilde I.; Van Zandbergen G.; Hartung T.; Solbach W.; Laskay T.
CORPORATE SOURCE: T. Laskay, Inst. for Med. Microbiol. and Hyg., University of Lubeck, Ratzeburger Allee 160, D-23538 Lubeck, Germany. Tamas.Laskay@hygiene.ukl.mu-luebeck.de
SOURCE: Journal of Leukocyte Biology, (2004) 75/3 (467-477).
Refs: 68
ISSN: 0741-5400 CODEN: JLBIE7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB . . . (LTA) is a major component of the cell membrane of gram-positive

bacteria. Although LTA has become increasingly recognized as an **immunomodulator**, its effect on **polymorphonuclear** neutrophil granulocytes (PMN) is still not clear. The interaction between LTA and PMN, however, is of particular importance, as PMN. . . . therefore, increased the lifespan of PMN. Experiments using blocking antibodies revealed that CD14 and Toll-like receptor 2 (TLR2) but not **TLR4** play a major role in LTA-mediated effects on PMN. These data clearly show that LTA, a component of gram-positive bacteria,. . . .

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ACCESSION NUMBER: 2004252016 EMBASE
TITLE: Role of Toll-like receptor 4 in the initiation and progression of atherosclerotic disease.
AUTHOR: Pasterkamp G.; Van Keulen J.K.; De Kleijn D.P.V.
CORPORATE SOURCE: Dr. G. Pasterkamp, Experimental Cardiology Laboratory, University Medical Centre (G02 523), Heidelberglaan 100, 3584 CX Utrecht, Netherlands. g.pasterkamp@hli.azu.nl
SOURCE: European Journal of Clinical Investigation, (2004) 34/5 (328-334).
Refs: 74
ISSN: 0014-2972 CODEN: EJCIB8
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The family of Toll-like receptors (TLRs) initiates an innate **immune** response after recognition of pathogen-associated molecular patterns (PAMPs). Evidence is accumulating that TLRs, and particularly **TLR4**, are important players in the initiation and progression of atherosclerotic disease. Not only exogenous ligands but also endogenous ligands that are expressed during arterial injury are recognized by **TLR4**. Mouse knockout studies and epidemiological studies of human **TLR4 polymorphisms** have demonstrated that the **TLR4** might play a role in the initiation and progression of atherosclerosis. This review will summarize the latest progression in research on the role of **TLR4** in arterial occlusive disease In addition, the potential of intervention in **TLR4** signalling to influence progression of atherosclerotic disease is discussed.

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ACCESSION NUMBER: 2004114831 EMBASE
TITLE: An association study of asthma and total serum immunoglobulin E levels for Toll-like receptor polymorphisms in a Japanese population.
AUTHOR: Noguchi E.; Nishimura F.; Fukai H.; Kim J.; Ichikawa K.; Shibasaki M.; Arinami T.
CORPORATE SOURCE: E. Noguchi, Department of Medical Genetics, Institute of Basic Medical Sciences, University of Tsukuba, Tsukuba, Ibaraki-ken 305-8575, Japan. mo00f210@md.tsukuba.ac.jp
SOURCE: Clinical and Experimental Allergy, (2004) 34/2 (177-183).
Refs: 35
ISSN: 0954-7894 CODEN: CLEAEN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
017 Public Health, Social Medicine and Epidemiology
022 Human Genetics
026 Immunology, Serology and Transplantation

LANGUAGE: English

SUMMARY LANGUAGE: English

AB . . . be explained by the hygiene hypothesis, which states that exposure to specific infections or endotoxins during infancy drives the maturing **immune** system towards a Th1 phenotype and away from the Th2 phenotype, which is associated with allergic diseases. Toll-like receptors (TLRs) play important roles in the signalling of many pathogen-related molecules and endogenous proteins associated with **immune** activation. Objective: The aim of the present study was to investigate whether **polymorphisms** in genes encoding TLRs are associated with asthma or total serum IgE levels. Methods: We screened the 5' flanking and coding regions of the TLR2, TLR3, **TLR4**, and TLR9 genes for **polymorphisms** by direct sequencing of DNA from 32 asthmatics, and analysed the effect of the **polymorphisms** on the development of atopic asthma and on total serum IgE levels. Results: We identified 16 variants in TLRs. The . . . none of the alleles or haplotypes were associated with asthma or total IgE levels ($P>0.05$). However, we found an insertion/deletion **polymorphism** in the 5' untranslated region of TLR2, and an expression construct containing the deletion allele showed lower luciferase activity than the wild-type alleles, suggesting that the deletion allele has reduced transcriptional activity. Conclusion: Our results indicate that **polymorphisms** in TLRs are not likely to be associated with the development of atopy-related phenotypes in a Japanese population.

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ACCESSION NUMBER: 2004192471 EMBASE

TITLE: A novel assay to detect nucleotide receptor P2X(7) genetic polymorphisms influencing numerous innate immune functions.

AUTHOR: Denlinger L.C.; Schell K.; Angelini G.; Green D.;
Guadarrama A.; Prabhu U.; Coursin D.B.; Hogan K.; Bertics P.J.

CORPORATE SOURCE: Dr. L.C. Denlinger, Div. of Pulmonary/Critical Care Med.,
Univ. of Wisconsin Medical School, 600 Highland Ave,
Madison, WI 53792, United States. ldenling@wisc.edu

SOURCE: Journal of Endotoxin Research, (2004) 10/2 (137-142).

Refs: 26

ISSN: 0968-0519 CODEN: JENREB

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

025 Hematology

026 Immunology, Serology and Transplantation

LANGUAGE: English

SUMMARY LANGUAGE: English

AB . . . pathways amplifying endotoxin responses has recently been highlighted by genetic studies describing LPS-hyporesponsive individuals despite carrying the common allele for **TLR4**. The nucleotide receptor P2X(7) modulates the production of numerous LPS-stimulated inflammatory mediators. We have recently described the largest phenotypic screen known for genetic **polymorphisms** associated with the nucleotide receptor P2X(7), a global regulator of leukocyte function. This required the development of a novel monocytic . . . P2X(7) alleles modulate LPS-stimulated cytokine production, and discusses a model wherein P2X(7) may serve as an amplification loop of innate **immunity**.
.COPYRGHT. W. S. Maney & Son Ltd.

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ACCESSION NUMBER: 2004168959 EMBASE

TITLE: Functional polymorphisms in LPS receptors CD14 and TLR4 are not associated with disease susceptibility or Campylobacter jejuni infection in Guillain-Barre patients.

AUTHOR: Geleijns K.; Jacobs B.C.; Van Rijs W.; Tio-Gillen A.P.;

CORPORATE SOURCE: Laman J.D.; Van Doorn P.A.
 K. Geleijns, Department of Neurology, Erasmus Medical
 Centre, Dr. Molewaterplein 50, Rotterdam 3015 GE,
 Netherlands. c.geleijns@erasmusmc.nl
 SOURCE: Journal of Neuroimmunology, (2004) 150/1-2 (132-138).
 Refs: 38
 ISSN: 0165-5728 CODEN: JNRIDW
 PUBLISHER IDENT.: S 0165-5728(04)00011-6
 COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 004 Microbiology
 008 Neurology and Neurosurgery
 022 Human Genetics
 026 Immunology, Serology and Transplantation
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB Guillain-Barre syndrome (GBS) is an acute **immune**-mediated
 polyneuropathy preceded by infections. Campylobacter jejuni is the most
 frequent pathogen and its lipopolysaccharide (LPS) induces antibodies
 cross-reactive with gangliosides. In this study we assessed whether known
 functional **polymorphisms** in the LPS receptors CD14 and Toll-like
 receptor 4 (**TLR4**) are associated with an increased
 susceptibility for GBS or with C. jejuni serology or C. jejuni related
 clinical and serological features. Comparison of the genotypes of 242 GBS
 patients and 210 healthy subjects showed that **polymorphisms** in
 CD14 and **TLR4** did not confer disease susceptibility and were not
 associated with C. jejuni infection. .COPYRGT. 2004 Elsevier B.V. All
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ACCESSION NUMBER: 2004048030 EMBASE
 TITLE: Polymorphisms of toll-like receptor 2 and 4 genes in
 rheumatoid arthritis and systemic lupus erythematosus.
 AUTHOR: Sanchez E.; Orozco G.; Lopez-Nevot M.A.; Jimenez-Alonso J.;
 Martin J.
 CORPORATE SOURCE: Dr. J. Martin, Inst. Parasitol. Biomedicina L., CSIC,
 C/Ventanilla no 11, 18001 Granada, Spain.
 martin@ipb.csic.es
 SOURCE: Tissue Antigens, (2004) 63/1 (54-57).
 Refs: 23
 ISSN: 0001-2815 CODEN: TSANA2
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 005 General Pathology and Pathological Anatomy
 022 Human Genetics
 026 Immunology, Serology and Transplantation
 031 Arthritis and Rheumatism
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB Human toll-like receptors (TLRs) participate in the innate response and
 signal the activation of adaptive **immunity**. Therefore, these
 TLRs may be important in autoimmune diseases such as rheumatoid arthritis
 (RA) and systemic lupus erythematosus (SLE). We investigated, by using a
 polymerase chain reaction restriction-fragment length **polymorphism**
 method, the possible association between the **polymorphisms** of
 TLR2 (Arg677Trp and Arg753Gln) and **TLR4** (Asp299Gly and
 Thr399Ile) genes with the susceptibility or severity of RA and SLE. Our
 study population consisted of 122 patients with SLE, 224 patients with RA,
 and a control group of 199 healthy individuals. The TLR2
polymorphisms were very rare in our population; no individual
 carrying the TLR2-Arg677Trp **polymorphism** was observed, whereas
 the TLR2-Arg753Gln **polymorphism** was present in only 1% of the
 total population. We found no statistically significant differences in the
TLR4-Asp299Gly and the **TLR4**-Thr399Ile genotype or allele

distribution between SLE patients, RA patients, and control individuals. Similarly, no association was found with any of. . . SLE patients. In conclusion, a case-control study was used to analyze, for the first time, the influence of TLR2 and **TLR4** gene **polymorphism** on the predisposition and clinical characteristics of SLE and RA but provided no evidence for association of TLR2 or **TLR4** gene **polymorphism** with either disease in the population under study.

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ACCESSION NUMBER: 2003358999 EMBASE
TITLE: Haplotype variation in bovine Toll-like receptor 4 and computational prediction of a positively selected ligand-binding domain.
AUTHOR: White S.N.; Taylor K.H.; Abbey C.A.; Gill C.A.; Womack J.E.
CORPORATE SOURCE: J.E. Womack, MS 4467, TAMU, College Station, TX 77843, United States. jwomack@cvm.tamu.edu
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2 Sep 2003) 100/18 (10364-10369).
Refs: 34
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Toll-like receptor 4 (**TLR4**) is a cell-surface receptor that activates innate and adaptive **immune** responses. Because it recognizes a broad class of pathogen-associated molecular patterns presented by lipopolysaccharides and lipoteichoic acid, **TLR4** is a candidate gene for resistance to a large number of diseases. In particular, mouse models suggest **TLR4** as a candidate gene for resistance to major agents in bovine respiratory disease and Johne's disease. The coding sequence of bovine **TLR4** is divided into three exons, with intron/ exon boundaries and intron sizes similar to those of human **TLR4** transcript variant 1. We amplified each exon in 40 individuals from 11 breeds and screened the sequence for single-nucleotide **polymorphisms** (SNPs). We identified 32 SNPs, 28 of which are in the coding sequence, for an average of one SNP per. . . that 12 SNPs need to be genotyped to distinguish these 20 haplotypes. These data provide a basic understanding of bovine **TLR4** sequence variation and supply haplotype markers for disease association studies.

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ACCESSION NUMBER: 2003209099 EMBASE
TITLE: Variants of toll-like receptor 4 modify the efficacy of statin therapy and the risk of cardiovascular events.
AUTHOR: Boekholdt S.M.; Agema W.R.P.; Peters R.J.G.; Zwinderman A.H.; Van der Wall E.E.; Reitsma P.H.; Kastelein J.J.P.; Jukema J.W.
CORPORATE SOURCE: Dr. J.W. Jukema, Department of Cardiology, Leiden University Medical Center, C5-P, Albinusdreef 2, 2300 RC Leiden, Netherlands. j.w.jukema@lumc.nl
SOURCE: Circulation, (20 May 2003) 107/19 (2416-2421).
Refs: 33
ISSN: 0009-7322 CODEN: CIRCAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
022 Human Genetics
037 Drug Literature Index
LANGUAGE: English

SUMMARY LANGUAGE: English

AB . . . Atherosclerosis is increasingly considered to be a chronic inflammatory process. We examined whether genetic variants of the toll-like receptor 4 (TLR4), which are correlated with impaired innate immunity and with progression of carotid atherosclerosis, are also associated with coronary atherosclerosis and predict the risk of cardiovascular events. Methods and Results - Two polymorphisms of the TLR4 gene (Asp299Gly and Thr399Ile) were determined in 655 men with angiographically documented coronary atherosclerosis. All patients participated in a prospective. . . reduced from 29.6% to 2.0% (P=0.0002, P=0.025 for interaction). Conclusions - Among symptomatic men with documented coronary artery disease, the TLR4 Asp299Gly polymorphism was associated with the risk of cardiovascular events. This variant also modified the efficacy of pravastatin in preventing cardiovascular events, . . .

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ACCESSION NUMBER: 2003181234 EMBASE
TITLE: Impaired expression of peroxisome proliferator-activated receptor γ in ulcerative colitis.
AUTHOR: Dubuquoy L.; A Jansson E.; Deeb S.; Rakotobe S.; Karoui M.; Colombel J.-F.; Auwerx J.; Pettersson S.; Desreumaux P.
CORPORATE SOURCE: Dr. P. Desreumaux, Service de Gastroenterologie, Hopital Huriez, CHU, Lille 59037, France. pdesreumaux@chru-lille.fr
SOURCE: Gastroenterology, (1 May 2003) 124/5 (1265-1276).
Refs: 46
ISSN: 0016-5085 CODEN: GASTAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB . . . aimed to determine the role of bacteria and their signaling effects on PPAR γ regulation during inflammatory bowel disease (IBD). Methods: TLR4-transfected Caco-2 cells, germ-free mice, and mice devoid of functional TLR4 (Lps(d)/ Lps(d) mice) were assessed for their expression of PPAR γ in colonic tissues in the presence or absence of bacteria. This nuclear receptor expression and the polymorphisms of gene also were assessed in patients with Crohn's disease (CD) and ulcerative colitis (UC), 2 inflammatory bowel diseases resulting from an abnormal immune response to bacterial antigens. Results: TLR4-transfected Caco-2 cells showed that the TLR4 signaling pathway elevated PPAR γ expression and a PPAR γ -dependent reporter in an I κ B dependent fashion. Murine and human intestinal flora induced. . .

L9 ANSWER 13 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2004020682 EMBASE
TITLE: TLR4 signaling induces TLR2 expression in endothelial cells via neutrophil NADPH oxidase.
AUTHOR: Fan J.; Frey R.S.; Malik A.B.
CORPORATE SOURCE: A.B. Malik, Department of Pharmacology, Univ. of Illinois Coll. of Medicine, 835 South Wolcott Avenue, Chicago, IL 60612, United States. abmalik@uic.edu
SOURCE: Journal of Clinical Investigation, (2003) 112/8 (1234-1243).
Refs: 60
ISSN: 0021-9738 CODEN: JCINAO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation

029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Interactions **polymorphonuclear** neutrophils (PMNs) with endothelial cells may contribute to the activation of endothelial cell responses involved in innate **immunity**. We explored a novel function of PMN NADPH oxidase in the mechanism of Toll-like receptor-2 (TLR2) upregulation induced by LPS-**TLR4** signaling in endothelial cells. We showed that LPS induced TLR2 up-regulation through **TLR4**-and MyD88-dependent signaling. In neutropenic mice, the LPS-induced NF-kB activation and TLR2 expression were significantly reduced, and both responses were restored. . . endothelial cells were secondary to oxidant signaling generated by PMN NADPH oxidase. The functional relevance of NADPH oxidase in mediating **TLR4**-induced TLR2 expression in endothelial cells was evident by markedly elevated and stable ICAM-1 expression as well as augmented PMN migration. . . challenge with LPS and peptidoglycan. Thus, PMN NADPH oxidase-derived oxidant signaling is an important determinant of the cross talk between **TLR4** and TLR2 and the control of endothelial cell activation.

L9 ANSWER 14 OF 28 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003422245 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12773319
TITLE: The role of innate immunity in acute allograft rejection after lung transplantation.
COMMENT: Comment in: Am J Respir Crit Care Med. 2003 Sep 15;168(6):623-4. PubMed ID: 12963577
Comment in: Am J Respir Crit Care Med. 2004 Apr 15;169(8):971; author reply 971-2. PubMed ID: 15072988
AUTHOR: Palmer Scott M; Burch Laurantell H; Davis R Duane; Herczyk Walter F; Howell David N; Reinsmoen Nancy L; Schwartz David A
CORPORATE SOURCE: Department of Medicine, Duke University Medical Center, Durham, NC, USA.. Palme002@mc.duke.edu
CONTRACT NUMBER: ES07498 (NIEHS)
ES11375 (NIEHS)
HL66604 (NHLBI)
HL66611 (NHLBI)
HL69978 (NHLBI)
SOURCE: American journal of respiratory and critical care medicine, (2003 Sep 15) 168 (6) 628-32.
Journal code: 9421642. ISSN: 1073-449X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030910
Last Updated on STN: 20031018
Entered Medline: 20031017

AB . . . responses independent of adaptive immunity, it remains unstudied in the context of transplant rejection. To investigate the role of innate **immunity** in the development of allograft rejection, we assessed the impact of two functional **polymorphisms** in the toll-like receptor 4 (**TLR4**) associated with endotoxin hyporesponsiveness on the development of acute rejection after human lung transplantation. Patients and donors were screened for. . .

L9 ANSWER 15 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2003329982 EMBASE
TITLE: TLR4 gene variants modify endotoxin effects on asthma.
AUTHOR: Werner M.; Topp R.; Wimmer K.; Richter K.; Bischof W.; Wjst M.; Heinrich J.
CORPORATE SOURCE: Dr. J. Heinrich, GSF Natl. Res. Ctr. Environ./Hlth.,

Institute of Epidemiology, Ingolstaedter Landstrasse 1,
D-85764 Neuherberg, Germany
SOURCE: Journal of Allergy and Clinical Immunology, (1 Aug 2003)
112/2 (323-330).
Refs: 37
ISSN: 0091-6749 CODEN: JACIBY
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
017 Public Health, Social Medicine and Epidemiology
022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background: Environmental exposure to endotoxin might have a crucial role in **immune** maturation and development of asthma. Objective: The aim of this study was to investigate whether the effect of endotoxin concentration in settled house dust on asthma is modified by the presence of variation in the **TLR4** gene. Methods: We performed a cross-sectional study within the German follow-up of the European Community Respiratory Health Survey. Multivariate logistic. . . between endotoxin exposure and diagnosed asthma, related clinical symptoms, and bronchial hyperreactivity (BHR) stratified for noncarriers and carriers of G299/I399 **polymorphism** in the **TLR4** gene. Results: In the noncarrier group (n = 279), the prevalence of asthma was significantly increased with elevated endotoxin levels. . . tertile, and 4.54 (95% CI, 0.94-21.96) in the third tertile compared with the lowest endotoxin tertile. The carriers of the **polymorphisms** (n = 55) showed a non-significant trend to have a lower risk of asthma (crude odds ratio, 0.67; 95% CI, . . . third tertile). We found a similar association for wheeze and endotoxin exposure that was also attenuated in subjects with G299/I399 **polymorphisms**. Conclusions: The G299/I399 **polymorphisms** were associated with a modified response to endotoxin, but the functional relationship still needs clarification.

L9 ANSWER 16 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2003131370 EMBASE
TITLE: Toll-like receptor-4 (TLR4) signaling augments chemokine-induced neutrophil migration by modulating cell surface expression of chemokine receptors.
AUTHOR: Fan J.; Malik A.B.
CORPORATE SOURCE: A.B. Malik, Department of Pharmacology, Univ. of Illinois Coll. of Medicine, Chicago, IL, United States.
abmalik@uic.edu
SOURCE: Nature Medicine, (1 Mar 2003) 9/3 (315-321).
Refs: 37
ISSN: 1078-8956 CODEN: NAMEFI
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Polymorphonuclear** leukocytes (PMNs) are critical effector cells of the innate **immune** system that protect the host by migrating to inflammatory sites and killing pathogenic microbes. We addressed the role of chemokine. . . The reduced expression of GRKs lowers chemokine receptor desensitization and markedly augments the PMN migratory response. These data indicate that **TLR4** modulation of PMN surface chemokine receptor expression subsequent to the downregulation of GRK2 and GRK5 expression is a critical determinant. . .

L9 ANSWER 17 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2003363807 EMBASE

TITLE: TLR4 Asp299Gly polymorphism is not associated with coronary artery stenosis.

AUTHOR: Yang I.A.; Holloway J.W.; Ye S.

CORPORATE SOURCE: I.A. Yang, Human Genetics Division, Univ. of Southampton Sch. of Med., Tremona Road, Southampton SO16 6YD, United Kingdom. i.yang@soton.ac.uk

SOURCE: Atherosclerosis, (1 Sep 2003) 170/1 (187-190).
Refs: 24
ISSN: 0021-9150 CODEN: ATHSBL

COUNTRY: Ireland

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
022 Human Genetics

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Inflammation and innate **immunity** may play a role in the pathogenesis of atherosclerosis. The Asp299Gly **polymorphism** in the toll-like receptor 4 (TLR4) gene reduces responsiveness to lipopolysaccharide and has been associated with reduced incidence and slower progression of carotid atherosclerosis. We analyzed this **polymorphism** in relation to susceptibility to and severity of coronary artery disease. Methods: 1400 participants (mean age: 63 years, 31% female) in the Southampton Atherosclerosis Study were genotyped for the TLR4 Asp299Gly **polymorphism** using the tetra-primer PCR method. Results: There was no significant difference between the frequencies of the Asp/Gly or Gly/Gly genotypes. . . . genotype groups and cardiac risk factors (P>0.05). Conclusion: The findings of this study do not support the hypothesis that the TLR4 Asp299Gly **polymorphism** influences predisposition to and progression of coronary artery disease. .COPYRGT. 2003 Elsevier Ireland Ltd. All rights reserved.

L9 ANSWER 18 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2003257419 EMBASE

TITLE: Toll-like receptor 4 and atherogenesis.

AUTHOR: Kiechl S.; Wiedermann C.J.; Willeit J.

CORPORATE SOURCE: Dr. S. Kiechl, Department of Neurology, Innsbruck University Clinic, Anichstr. 35, A-6020 Innsbruck, Austria. Stefan.Kiechl@uibk.ac.at

SOURCE: Annals of Medicine, (2003) 35/3 (164-171).
Refs: 40
ISSN: 0785-3890 CODEN: ANMDEU

COUNTRY: Norway

DOCUMENT TYPE: Journal; (Short Survey)

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Toll-like receptor 4 (TLR4) is a pattern recognition receptor involved in the innate **immune** response to various micro-organisms and other exogenous and endogenous stress factors. Recently, evidence emerged that important inflammatory processes implicit in human atherogenesis are mediated in part via the TLR4/nuclear factor- κ B pathway. **Polymorphisms** of TLR4, which attenuate receptor signalling, enhance the risk of acute severe infections but may have opposite effects on atherogenesis. The aim of this review is to critically discuss current experimental and epidemiological evidence for a role of TLR4 in atherogenesis and to highlight the main controversies and perspectives in this emerging field of vascular biology.

L9 ANSWER 19 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2003234081 EMBASE
TITLE: Rapid and reliable genotyping for the Toll-like receptor 4
A896G polymorphism using fluorescence-labeled hybridization
probes in a real-time polymerase chain reaction assay.
AUTHOR: Heesen M.; Wessiepe M.; Kunz D.; Vasickova K.; Blomeke B.
CORPORATE SOURCE: M. Heesen, Department of Anesthesia, Academic Medical
Center, University of Amsterdam, Meibergdreef 9, 1100 DD
Amsterdam, Netherlands. m.heesen@amc.uva.nl
SOURCE: Clinica Chimica Acta, (1 Jul 2003) 333/1-2 (47-49).
Refs: 10
ISSN: 0009-8981 CODEN: CCATAR
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
027 Biophysics, Bioengineering and Medical
Instrumentation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background: The Toll-like receptor 4 (TLR4) is involved in
immune response to endotoxin as well as the pathogenesis of
atherosclerosis. The TLR4 gene was shown to carry a
single-nucleotide polymorphism (A896G). We developed a
rapid-cycle polymerase chain reaction (PCR) which allows for rapid
genotyping and, therefore, may be useful in. . . German Caucasians were
genotyped. The interleukin-1 β (IL-1 β) response to endotoxin was
assessed after whole blood stimulation with endotoxin according to
TLR4 genotypes. Results: The method suggested by us is a
time-saving technique requiring no additional manual steps. Frequencies of
the A. . . levels were lower in carriers of the G allele. Conclusions:
This PCR assay is a rapid and reliable technique for TLR4
genotyping. .COPYRGT. 2003 Elsevier Science B.V. All rights reserved.

L9 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:302273 CAPLUS
DOCUMENT NUMBER: 138:383635
TITLE: Genetic polymorphism and tumor immunotherapy
AUTHOR(S): Yang, Rongcun; Roden, Richard B. S.
CORPORATE SOURCE: Department of Pathology, The Johns Hopkins School of
Medicine, Baltimore, MD, 21205, USA
SOURCE: Current Pharmacogenomics (2003), 1(1), 37-57
CODEN: CPUHAC; ISSN: 1570-1603
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 236 THERE ARE 236 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

ST review polymorphism tumor immunotherapy cytokine
TLR4 receptor

L9 ANSWER 21 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2002362636 EMBASE
TITLE: Polymorphisms of TLR4: Rapid genotyping and reduced
response to lipopolysaccharide of TLR4 mutant alleles.
AUTHOR: Schmitt C.; Humeny A.; Becker C.-M.; Brune K.; Pahl A.
CORPORATE SOURCE: A. Pahl, Inst. fur Pharmakol./Toxikologie, Universitat
Erlangen, Fahrstrasse 17, D-91054 Erlangen, Germany.
pahl@pharmakologie.uni-erlangen.de
SOURCE: Clinical Chemistry, (1 Oct 2002) 48/10 (1661-1667).
Refs: 49
ISSN: 0009-9147 CODEN: CLCHAU

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background: Pathogen recognition receptors such as Toll-like receptors (TLRs), which recognize pathogen-associated molecular patterns, lead to the activation of innate **immunity**. Genetic variations in these receptors may lead to an altered host **immune** response to pathogens. Methods: We developed homogeneous fluorescence-based PCR assays as well as matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) genotyping assays to detect **TLR4 polymorphisms**. These assays were compared with restriction fragment length **polymorphism** (RFLP) analysis. Peripheral blood monocytes from donors with differing genotypes were prepared and exposed to bacterial products in vitro. The . . . monocytes were monitored by real-time reverse transcription-PCR. Results: By our homogeneous PCR method, the allele frequencies were 5.6% for the **TLR4** Asp299Gly and 6.0% for the **TLR4** Thr399Ile **polymorphism** in 116 healthy German Caucasians. Nine incorrect genotype calls were detected in the RFLP analysis and two in the TaqMan genotype analysis. MALDI-TOF-MS allowed clear detection of all **TLR4** alleles. Monocytes from donors homozygous for the **TLR4** mutant alleles Asp299Gly and Thr399Ile were lipopolysaccharide hyporesponsive and exhibited median effective concentrations (EC(50)s) approximately fourfold higher than those of monocytes carrying wild-type or heterozygous alleles. In contrast, a TLR2 agonist elicited similar responses in monocytes irrespective of the **TLR4** genotype. Conclusions: Homogeneous fluorescence-based PCR assays provide a specific and sensitive method for high-throughput genotyping of **TLR4** mutations. The newly developed PCR and MALDI-TOF-MS assays may be useful to evaluate the presence of **TLR4 polymorphisms** in patients to predict susceptibility to bacterial infection. .COPYRGT. 2002 American Association for Clinical Chemistry.

L9 ANSWER 22 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2002413262 EMBASE
TITLE: The CARD15 2936insC mutation and TLR4 896 A>G polymorphism in African Americans and risk of preterm premature rupture of membranes (PPROM).
AUTHOR: Ferrand P.E.; Fujimoto T.; Chennathukuzhi V.; Parry S.; Macones G.A.; Sammel M.; Kuivaniemi H.; Romero R.; Strauss III J.F.
CORPORATE SOURCE: J.F. Strauss III, Ctr. for Res. Reprod./Women's Hlth., University of Pennsylvania, 421 Curie Boulevard, Philadelphia, PA 19104, United States. jfs3@mail.med.upenn.edu
SOURCE: Molecular Human Reproduction, (1 Nov 2002) 8/11 (1031-1034).
Refs: 27
ISSN: 1360-9947 CODEN: MHREFD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
010 Obstetrics and Gynecology
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB . . . to initiate tissue responses leading to PPRM in the setting of Gram negative infection. LPS is recognized by the innate **immune** system, including the proteins encoded by the CARD15 and **TLR4** genes. A recently described mutation (2936insC) in CARD15 and a

polymorphism in **TLR4** 896 A>G impair responses to LPS. The objective of this study was to determine if African Americans, who have a higher incidence of PPRM than Caucasians, have different frequencies of the mutant CARD15 allele and the **TLR4** hyporesponsive variant, and if risk of PPRM is influenced by fetal carriage of these alleles. The allele frequencies for the CARD15 mutation and the **TLR4** 896G variant in African Americans were similar to those reported for Caucasians. There was no association between the **TLR4** alleles examined and PPRM. However, the CARD15 mutation was only detected in controls and not in PPRM cases. We conclude that the CARD15 mutation and hyporesponsive **TLR4** allele do not contribute to ethnic variation in the incidence of PPRM.

L9 ANSWER 23 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2002302600 EMBASE
TITLE: Association between the Asp299Gly polymorphisms in the toll-like receptor 4 and premature births in the Finnish population.
AUTHOR: Lorenz E.; Hallman M.; Marttila R.; Haataja R.; Schwartz D.A.
CORPORATE SOURCE: Dr. E. Lorenz, Department of Medicine, Wake Forest University, School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, United States. elorenz@wfubmc.edu
SOURCE: Pediatric Research, (2002) 52/3 (373-376).
Refs: 21
ISSN: 0031-3998 CODEN: PEREBL
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
017 Public Health, Social Medicine and Epidemiology
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB . . . increases the cost for neonatal care. Urogenital infection, often caused by Gram-negative bacteria, is a known risk factor. Toll-like receptor-4 (**TLR4**) is the major endotoxin-signaling receptor and as such is crucial for the initiation of the innate **immune** response against Gram-negative bacteria. Recently, a variant in the human **TLR4** gene was shown to be associated with impaired receptor function and an increased likelihood of Gram-negative sepsis. In the present study, we determined whether the same **polymorphism** in **TLR4** gene is associated with an increased risk for premature birth. We analyzed genotypes for a Finnish study population consisting of . . . and 440 premature infants (gestational age <35 wk; 282 single-tons, 158 multiples) and 94 mothers for the presence of the **TLR4** **polymorphisms** Asp299Gly and Thr399Ile. These **polymorphisms** were in linkage disequilibrium. The 299Gly allele frequencies were 10.6% (93 of 880) in premature infants and 8.3% (58 of . . . of 345) of term infants and 15.0% (3 of 20) of the mothers delivering at term were carriers of the **TLR4** variant. The frequencies of 299Gly allele and Asp/Gly or Gly/Gly genotype carrier status in premature singleton infants were higher than. . . in premature multiples (p = 0.036, p = 0.044, respectively). According to the present results an allelic variation in the **TLR4** receptor was associated with increased risk of premature birth.

L9 ANSWER 24 OF 28 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002300020 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12040919
TITLE: TLR4 and LPS hyporesponsiveness in humans.
AUTHOR: Schwartz David A
CORPORATE SOURCE: Pulmonary and Critical Care Division, Department of Internal Medicine, Department of Genetics, Department of

Veterans Affairs Medical Center, Duke University Medical
Center, Durham, NC, USA.. david.schwartz@duke.edu
CONTRACT NUMBER: ES07498 (NIEHS)
ES09607 (NIEHS)
HL62628 (NHLBI)
HL64855 (NHLBI)
SOURCE: International journal of hygiene and environmental health,
(2002 Apr) 205 (3) 221-7.
Journal code: 100898843. ISSN: 1438-4639.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20020604
Last Updated on STN: 20021211
Entered Medline: 20021119

AB . . . indicates that both acquired and innate immune responses in the lung may be influenced by polymorphic genes. For instance, functional **polymorphisms** in the IL-4 receptor gene are thought to preferentially stimulate acquired Th2 **immune** responses to inhaled allergens, and we have recently shown that common co-segregating mutations in **TLR4** (a transmembrane receptor for LPS) are associated with diminished airway responsiveness to inhaled LPS. These observations suggest that environmental challenges. . .

L9 ANSWER 25 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:141275 BIOSIS
DOCUMENT NUMBER: PREV200200141275
TITLE: **Polymorphisms** of the **immune** regulatory genes cytotoxic-lymphocyte antigen-4 (CTLA-4), Toll-like receptor 4 (**TLR4**) and transforming growth factor beta (TGFbeta) in the development of autoimmune hepatitis type 1.
AUTHOR(S): Kassi, Delia [Reprint author]; Lohse, Ansgar W.; Galle, Peter R.; Hoehler, Thomas
CORPORATE SOURCE: Johannes Gutenberg University Mainz, Mainz, Germany
SOURCE: Hepatology, (October, 2001) Vol. 34, No. 4 Pt. 2, pp. 530A. print.
Meeting Info.: 52nd Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases. Dallas, Texas, USA. November 09-13, 2001.
CODEN: HPTLD9. ISSN: 0270-9139.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2002
Last Updated on STN: 26 Feb 2002

TI **Polymorphisms** of the **immune** regulatory genes cytotoxic-lymphocyte antigen-4 (CTLA-4), Toll-like receptor 4 (**TLR4**) and transforming growth factor beta (TGFbeta) in the development of autoimmune hepatitis type 1.
GEN human CTLA4 gene [human cytotoxic T lymphocyte antigen-4 gene] (Hominidae): immunoregulatory gene, polymorphisms; human Toll-like receptor 4 gene [human **TLR4** gene] (Hominidae): **immunoregulatory** gene, **polymorphisms**; human transforming growth factor-beta gene [human TGF-beta gene] (Hominidae): immunoregulatory gene, polymorphisms

L9 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:77984 CAPLUS
DOCUMENT NUMBER: 137:45916
TITLE: The role of TLR4 in endotoxin responsiveness in humans
AUTHOR(S): Schwartz, David A.
CORPORATE SOURCE: Pulmonary and Critical Care Division, Department of

Medicine and the Department of Veterans Affairs
Medical Center and Duke University Medical Center,
Durham, NC, 27710, USA
SOURCE: Journal of Endotoxin Research (2001), 7(5), 389-393
CODEN: JENREB; ISSN: 0968-0519
PUBLISHER: Maney Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Alleles
Human
Immune tolerance
Signal transduction, biological
Stress, animal
(TLR4 receptor gene polymorphism role in response
to inhaled endotoxin in humans)

L9 ANSWER 27 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2002090973 EMBASE
TITLE: Polymorphisms in the tumor necrosis factor (TNF) genes are
associated with susceptibility to effects of ultraviolet-B
radiation on induction of contact hypersensitivity.
AUTHOR: Niizeki H.; Naruse T.; Hecke K.H.; Taylor J.R.; Kurimoto
I.; Shimizu T.; Yamasaki Y.; Inoko H.; Streilein J.W.
CORPORATE SOURCE: Dr. H. Niizeki, Department of Dermatology, National Tokyo
Medical Center, 2-5-1 Higashi-ga-Oka, Meguro, Tokyo
152-8902, Japan. hniizeki@ntmc.hosp.go.jp
SOURCE: Tissue Antigens, (2001) 58/6 (369-378).
Refs: 39
ISSN: 0001-2815 CODEN: TSANA2
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We investigated the allelic distributions of single nucleotide
polymorphisms (SNPs) of the TNFA, TNFB and IKBL genes, 3
microsatellites within the tumor necrosis factor (TNF) region of HLA
locus, and the HLA phenotypes as well as the TLR4 gene in
Chromosome 9 in 26 healthy Caucasian volunteers. These individuals were
also assessed as ultraviolet B (UVB)-susceptible (S) or. . . the UVB
phenotypes failed. Similarly, attempts to correlate SNP at the NcoI-RFLP
within intron 1 of the TNFB, IKBL and TLR4 gene with UVB
phenotypes also failed. However, microsatellite analyses of TNFa, TNFc,
and TNFd markers revealed a significant increase in. . . a high
TNF- α responder, whereas TNFd3 is a TNF- α low responder, we
propose that the TNF region of HLA contains polymorphic genes
that confer susceptibility and resistance to the deleterious effects of
UVB radiation on the induction of contact hypersensitivity. This. . .
in mice contains alleles that dictate the UVB-dependent phenotypes in
mice, and implicate TNF- α as the primary mediator of the
immune-damaging effects of UVB radiation.

L9 ANSWER 28 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2000211258 EMBASE
TITLE: Differential expression and regulation of toll-like
receptors (TLR) in human leukocytes: Selective expression
of TLR3 in dendritic cells.
AUTHOR: Muzio M.; Bosisio D.; Polentarutti N.; D'Amico G.;
Stoppacciaro A.; Mancinelli R.; Van't Veer C.; Penton-Rol

CORPORATE SOURCE: G.; Ruco L.P.; Allavena P.; Mantovani A.
 Dr. M. Muzio, Dept. of Immunology and Cell Biology, Mario
 Negri Institute, via Eritrea 62, Milan I-20157, Italy.
 muziom@irfmn.mnegri.it
 SOURCE: Journal of Immunology, (2000) 164/11 (5998-6004).
 Refs: 24
 ISSN: 0022-1767 CODEN: JOIMA3
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 025 Hematology
 026 Immunology, Serology and Transplantation
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 AB Members of the Toll-like receptor (TLR) family probably play a fundamental
 role in pathogen recognition and activation of innate **immunity**.
 The present study used a systematic approach to analyze how different
 human leukocyte populations express specific transcripts for the first
 five characterized TLR family members. TLR1 was expressed in all
 leukocytes examined, including monocytes, **polymorphonuclear**
 leukocytes, T and B cells, and NK cells. In contrast TLR2, **TLR4**,
 and TLR5 were expressed in myelomonocytic elements. Exposure to bacterial
 products, such as LPS or lipoarabinomannan, or to proinflammatory
 cytokines increased **TLR4** expression in monocytes and
polymorphonuclear leukocytes, whereas IL-10 blocked this effect.
 TLR3 was only expressed in human dendritic cells (DC) wherein maturation
 induced by bacterial. . . full TLR repertoire. These data suggest that
 TLR can be classified based on expression pattern as ubiquitous (TLR1),
 restricted (TLR2, **TLR4**, and TLR5 in myelomonocytic cells), and
 specific (TLR3 in DC) molecules.

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

98.06

98.27

STN INTERNATIONAL LOGOFF AT 16:29:50 ON 14 JUL 2004